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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,353	02/26/2004	Arthur M. Krieg	C1039.70083US07	9688

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EXAMINER	
ARCHIE, NINA	

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/789,353	KRIEG ET AL.	
	Examiner	Art Unit	
	Nina A. Archie	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-34 and 36* is/are pending in the application.

4a) Of the above claim(s) *30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-29, 31-33 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 10/1/2007; 10/25/2007; 4/2/2007
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office Action is responsive to Applicant's amendment and response filed on 10/1/2007. Claims 28-36 are pending. Claims 28 and 29 have been amended. Claim 35 have been cancelled.

Information Disclosure Statement

2. The information disclosure statement filed on 4/27/2007, 10/1/2007, 10/29/2007, and 3/28/2007 has been considered. Initialed copies are enclosed.

Claim Rejections Withdrawn

3. In view of the Applicant's amendment and remark following objections are withdrawn.

a) Rejection of claims 28 and 35 under 35 U.S.C. 103(a) is withdrawn in light of applicant's argument.

b) Rejection of claim 36 under 35 U.S.C. 103(a) is withdrawn in light of applicant's argument.

Claim Rejections Maintained

Double Patenting

4. The rejection of claims 28 and 36 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 101, 107-109, 120-122, 124 of copending Application No. 10/314,578 are maintained for the reasons set forth in the previous office action.

Applicant arguments:

Claims 28 and 36 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 101, 107-109, 120-122, 124 of copending request No. 10/314,578. US Application No. 10/314,578 has

now issued as US Patent 7,271,156. The named inventors of US Application No. 10/314,578 are Arthur Krieg, Jorg Vollmer and Christian Schetter. The owners of the patent are University of Iowa Research Foundation and Coley Pharmaceutical GmbH. The rejection of claims 28 and 36 on the ground of nonstatutory obviousness-type double patenting is improper and should be withdrawn. The instant application is owned by University of Iowa Research Foundation, The United States of America, as represented by the Secretary, Department of Health and Human Services, and Coley Pharmaceutical Group Inc. US Application No. 10/314,578 is owned by University of Iowa Research Foundation and Coley Pharmaceutical GmbH. MPEP 804 II B(1)teaches that "obviousness-type double patenting requires rejection of an application claim when the claimed subject matter is not patentably distinct from the subject matter claimed in a commonly owned patent, or a non-commonly owned patent but subject to a joint research agreement as set forth in 35 USC 103(c)(2) and (3), when the issuance of a second patent would provide unjustified extension of the term of the right to exclude granted by a patent." Although the two patent applications have a common inventor and one owner in common, the applications are not commonly owned (common ownership requires all of the same owners). At the time of the instant invention the claimed invention was not assigned to or under an obligation of assignment to the University of Iowa Research Foundation and Coley Pharmaceutical GmbH, but rather was under an obligation of assignment to University of Iowa Research Foundation and the United States of America and was co-owned by Alfred Steinberg. At the time of the instant invention the claimed invention was not subject to a research agreement between the parties and the different owners of US Application No. 10/314,578. The instant application is not commonly owned or the subject of a joint research agreement with US Application No. 10/314,578. Thus, it is requested that the rejection be withdrawn.

Examiner's Response to Applicant's Arguements:

Examiner disagrees with Applicant's assertion because the inventions do not have common ownership, this rejection would maintain as a obviousness-double-

patenting rejection (see MPEP 804 Chart IIB).

New Grounds of Objections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 28-29, 31-33, and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuramoto et al 1992 Jpn J. Cancer Res Vol. 83 pgs. 1128-1131 in view of Goodchild et al 1990 The American Chemical Society, Vol. 1, No. 3 pgs. 165-182, Hutcherson et al US Patent 5,723,335 March 3, 1998 (filed March 25, 1994), and Cheng et al US Patent No. 5,646,126 July 8, 1997 (filed February 28, 1994).

Claims 28-29, 31-33, and 36 are drawn to an oligonucleotide, comprising: 5'-AACGTT-3', 8-40 nucleotides in length, wherein each internucleotide linkage has a phosphate backbone modification, wherein the phosphate backbone is a phosphorothioate.

Kuramato et al teach an oligonucleotide, comprising: 5'-AACGTT-3', 8-40 nucleotides in length.

Kuramoto et al teach that all oligonucleotide used were synthesized by the standard phosphoramidite method using an automatic DNA synthesizer.

Kuramato et al does not teach an oligonucleotide wherein internucleotide linkage has a phosphate backbone modification, wherein the phosphate backbone is a phosphorothioate, and having at least one phosphate backbone modification, wherein the oligonucleotide is linked to a nucleic acid delivery complex, wherein the oligonucleotide is covalently linked to the nucleic acid delivery complex, wherein the nucleic acid delivery complex is a cationic lipid, wherein the nucleic acid delivery complex is sterol. Kuramoto et al does not teach a composition of comprising the oligonucleotide and a pharmaceutically acceptable carrier.

Goodchild et al teaches an oligonucleotide wherein the phosphate backbone modification is a phosphorothioate (see pg. 167 column 1 last paragraph, column 2 last paragraph). Goodchild et al teaches that backbone modifications are utilized to improve the stability of the DNA to enzymatic degradation (see pg. 167 "Synthesis of Modified Oligonucleotides", pg. 175 "The Effect of Modification on Nuclease Resistance"). Goodchild et al. teaches that shorter oligonucleotides are taken up more rapidly (see pg. 176 column 1 paragraph 5).

Hutcherson et al teach a composition (see column 5 lines 40-67, column 6 lines 31-43, column 7 lines 55-67, column 10 lines 46-57) comprising: an oligonucleotide delivery complex, wherein the oligonucleotide delivery complex contains an immunostimulatory CpG containing oligonucleotide associated (covalently) with a cationic lipid, wherein the CpG includes a phosphate backbone modification is a

phosphorothioate (see abstract, column 5 lines 40-59, column 8 lines 31-50). Hutcherson et al teach a composition comprising a pharmaceutically acceptable carrier (see column 7 lines 49-55), wherein the oligonucleotide is synthetic (see column 8 lines 32-41).

Cheng et al teach oligonucleotides having phosphorothioate linkage covalently linked to a sterol.

It would have been prima facie obvious at the time the invention was made to modify the oligonucleotide of Kuramato et al by modifying the backbone and inclusion of linking the oligonucleotide in a delivery complex according to Hutcherson et al to because Hutcherson et al teaches that cationic lipids can significantly enhance the uptake and fate of oligonucleotides. It would also have been prima facie obvious to modify the backbone of the oligonucleotide of Kataoka et al to include phosphorothioate taught by Goodchild et al because Goodchild et al teaches that the backbone modifications prevent degradation by nucleases and increase or improve uptake (see section B pg. 167). It would have been prima facie obvious at the time the invention was made to modify the oligonucleotide of Kuramoto et al by inclusion of a sterol because both Cheng et al and Kuramato both teach oligonucleotide in a delivery complex.

6. Claims 28-29, 31-33, and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kataoka et al 1992 Jpn. J. Cancer Res. Vol. 83 pgs. 244-247 in view of Goodchild et al 1990 The American Chemical Society, Vol. 1, No. 3 pgs. 165-182, Hutcherson et al US Patent 5,723,335 March 3, 1998 (filed March 25, 1994), and Cheng et al US Patent No. 5,646,126 July 8, 1997 (filed February 28, 1994).

Claims 28-29, 31-33, and 36 are drawn to an oligonucleotide, comprising: 5'-TGACGTT-3', 8-40 nucleotides in length, wherein each internucleotide linkage has a phosphate backbone modification, wherein the phosphate backbone is a phosphorothioate.

Katoaka et al teach an oligonucleotide, comprising: 5'-TGACGTC-3' (BCG-A4a), 8-40 nucleotides in length.

Kataoka et al teaches that the oligonucleotide is synthesized by an automated DNA synthesizer and that the backbone is modified by the standard phosphoramiditie method as taught by Tokunaga et al. Tokunaga et al teach that the phosphate backbone modification is a phosphoramidite.

Katoaka et al does not teach an oligonucleotide wherein internucleotide linkage has a phosphate backbone modification, wherein the phosphate backbone is a phosphorothioate, and having at least one phosphate backbone modification, wherein the oligonucleotide is linked to a nucleic acid delivery complex, wherein the oligonucleotide is covalently linked to the nucleic acid delivery complex, wherein the nucleic acid delivery complex is a cationic lipid, wherein the nucleic acid delivery complex is sterol. Kuramoto et al does not teach a composition of comprising the oligonucleotide and a pharmaceutically acceptable carrier.

Goodchild et al teaches an oligonucleotide wherein the phosphate backbone modification is a phosphorothioate (see pg. 167 column 1 last paragraph, column 2 last paragraph). Goodchild et al teaches that backbone modifications are utilized to improve the stability of the DNA to enzymatic degradation (see pg. 167 "Synthesis of Modified Oligonucleotides", pg. 175 "The Effect of Modification on Nuclease Resistance"). Goodchild et al. teaches that shorter oligonucleotides are taken up more rapidly (see pg. 176 column 1 paragraph 5). Tokunaga et al. and Goodchild et al both teach backbone modifications.

Hutcherson et al teach a composition (see column 5 lines 40-67, column 6 lines 31-43, column 7 lines 55-67, column 10 lines 46-57) comprising: an oligonucleotide delivery complex, wherein the oligonucleotide delivery complex contains an immunostimulatory CpG containing oligonucleotide associated (covalently) with a cationic lipid, wherein the CpG includes a phosphate backbone modification is a phosphorothioate (see abstract, column 5 lines 40-59, column 8 lines 31-50). Hutcherson et al teach a composition comprising a pharmaceutically acceptable carrier

(see column 7 lines 49-55), wherein the oligonucleotide is synthetic (see column 8 lines 32-41).

Cheng et al teach oligonucleotides having phosphorothioate linkage covalently linked to a sterol.

It would have been prima facie obvious at the time the invention was made to modify the oligonucleotide of Katoaka et al by modifying the backbone and inclusion of linking the oligonucleotide in a delivery complex according to Hutcherson et al to because Hutcherson et al teaches that cationic lipids can significantly enhance the uptake and fate of oligonucleotides. It would also have been prima facie obvious to modify the backbone of the oligonucleotide of Kataoka et al to include phosphorothioate taught by Goodchild et al because Goodchild et al teaches that the backbone modifications prevent degradation by nucleases and increase or improve uptake (see section B pg. 167). It would have been prima facie obvious at the time the invention was made to modify the oligonucleotide of Katoaka et al by inclusion of a sterol because both Cheng et al teach that oligonucleotide in a delivery complex show selective toxicity toward certain specific cancer cells, including some cancer cells which have multiple drug resistance (MDR) against certain established cancer chemotherapeutic agents.

Status of the Claims

7. No claims allowed.

Claims 30 and 34 are withdrawn.

Claims 28-29, 32-33 and 36 are rejected.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nina A Archie
Examiner
GAU 1645
REM 3B31

MARK NAVARRO
PRIMARY EXAMINER